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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/126,559	07/30/1998	DANIEL J. CAPON	11068-043-999	9053

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 07/15/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/126,559	CAPON ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *112-116* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *112-116* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

1. Currently, claims 112-116 are pending and under consideration in the application. In the prior action, mailed on November 6, 2002, claims 1, 4, 8, 55, and 57 were pending and rejected. In the Response, filed on May 6, 2003, the Applicant cancelled claims 1, 4, 8, 55, and 57, and added new claim 112-116. These new claims are now pending and under consideration.

2. This action is being made Non-Final due to the presence of new rejections, raising new issues, and not necessitated by amendment.

Claim Rejections - 35 USC § 112

3. **(Prior Rejection- Withdrawn)** Claims 1,4, 8, 55, and 57 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejected claims have been cancelled from the application, and replaced by new claims 112-116. This rejection is withdrawn in view of these amendments to the claims, and in view of the Applicant's arguments therewith.

4. **(Prior Rejection- Withdrawn)** Claims 1,4, 8, 55, and 57 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejected claims

have been cancelled from the application, and replaced by new claims 112-116. The rejection is withdrawn in view of the amendments to the claims.

5. **(Prior Rejection- Withdrawn)** Claims 55 and 57 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims have been cancelled from the application, and have been replaced by new claims 115 and 116. The rejection of the claims is withdrawn in view of the amendment to the claimed method as represented by the new claims.

6. **(New Rejection-Necessitated by Amendment)** Claims 112-115 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of determining if a particular viral is susceptible to an anti-viral drug, does not reasonably provide enablement for methods of determining if a viral population is so susceptible. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to does not the invention commensurate in scope with these claims. The present claims read on methods of determining the susceptibility of an HCV population to an anti-viral drug based on the effect of the drug to a particular reporter cell line comprising a single HCV gene.

However, whereas a population of viruses may contain viruses of many different geno- and pheno-types, as claimed the current method is determining the effect of the drugs on only a single member of that population. At best, the currently claimed methods would be able to determine that a viral population, as a whole, is susceptible to an anti-viral drug. Such would be

the case if the particular clone tested were found to be so susceptible. Were the tested clone found not to be so susceptible, it would not demonstrate that none of the other members of the viral population are so susceptible. Therefore, the Applicant is not enabled for the methods of determining anti-viral drug susceptibility as claimed.

7. **(New Rejection)** Claims 112-116 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of determining HCV susceptibility to an anti-viral drug that inhibits or prevents viral replication, does not reasonably provide enablement for any anti-viral drug. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims have been described in part above. However, while the claimed methods would be operative for the determination of viral susceptibility to certain drugs that inhibit viral replication, the claims are not enabled for anti-HCV drugs that operate through means other than inhibiting viral replication.

While inhibitors of viral replication are recognized anti-HCV agents, they are not the only known anti-HCV drugs. For example, each of the patents 5,350,671 (671 patent) and 5,597,691 (691 patent) teach other examples of anti-HCV drugs. (Both patents are issued to Houghton et al.) The 671 patent indicates that both drugs that inhibit replication, and those that inhibit infection would be useful. Column 23, lines 32-40. The 691 patent indicates that inhibitors of the HCV protease responsible for cleavage of the HCV polyprotein would also be effective drugs. Col. 13, lines 16-32. However, the susceptibility of an HCV clone to such other

drugs would not be determined by the currently claimed method. Thus, the applicant is not enabled for the full scope of the claimed invention.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. **(Prior Rejection-Maintained)** Claims 1, 4, 8, and 57 were rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over U.S. Patent Number 6,127,116, issued to Rice et al. These claims have been cancelled from the application, and have been replaced by new claims 112-114, and 116. These claims differ from the cancelled claims by describing methods of determining the susceptibility of a hepatitis C virus population, rather than of determining susceptibility generally, to an anti-HCV drug. The steps of the methods are substantially the same to those described in the prior action.

In traversal of this rejection, the Applicant argues that the currently claimed methods are drawn to methods of determining the susceptibility of HCV populations, and not individual virus or sequences, to anti-HCV drugs. The Applicant argues that the Rice reference, "at best, proposes that individual sequences might be identified that are resistant to anti-HCV therapy." The Examiner is not persuaded by this argument.

The Applicant appears to be indicating that the current claims are not anticipated by the Rice reference because the current claims determine that HCV populations are resistant to anti-viral drugs, whereas the Rice reference teaches a method of only determining if individual HCV clones are resistant. However, it is noted that in each of the claims of the present application, the method involves host cell comprising "a patient-derived segment that comprises **a HCV gene**." See, e.g. claims 112, 115, and 116. None of these methods requires that more than a single HCV gene be tested for anti-viral drug resistance. As only a single gene is being tested, the methods are inherently testing for the susceptibility of only single virus genotype, those containing the particular gene being tested. Thus, the Rice reference is still anticipatory of the claimed methods.

It is also noted that the distinction that the Applicant is attempting to drawn between the methods as claimed and the method of Rice is in the conclusion that is made from the results of the method. However, it would have been obvious to those in the art that, if a particular virus from a patient is found either susceptible or not susceptible, then there would be at least a portion of the HCV population within that patient that shares that characteristic.

Furthermore, the Rice reference recognizes, and is partially reliant, on the existence and emergence of variant strains of HCV. See e.g., paragraph spanning columns 1-2 (recognizing the diversity of the viral genome, and the emergence of variants within an individual), and column 12, lines 9-17 (indicating the existence of adaptive mutations within a viral strain). In view of these teachings, it would have been obvious to one of ordinary skill in the art to have applies the methods described therein to multiple viral genotypes, including to multiple viral genotypes in an individual. Thus, even if the claims did read on methods of testing a population of viruses for

drug susceptibility, rather than a specific genotype, the Rice reference would still have rendered the claims obvious.

10. Claim 115 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rice as applied to claims 112-114, and 116 above, and further in view of the teachings of Fridland et al., U.S. patent 5,576,177, and Bornstein et al., Reissue 29,955. Claim 15 varies from the other claims in the application in that, instead of comparing the HCV gene expression in the presence of a drug with a control, the results are compared with a standard curve. The teachings of Rice have been described above, and in the prior action. The reference teaches the comparison of the gene expression in the presence of the drug, to a control where gene expression is measured in the absence of the drug. It does not teach the use of a standard curve.

However, the use of a standard curve rather than a repeated control is known in the art. See e.g. U.S. Patent 5,576,177, issued to Fridland et al., and U.S. Reissue 29,955, issued to Bornstein et al. Each of these references teaches the use of a standard curve from a control for later use in comparison of results in assays. Fridland, col. 12, lines 16-29; and Bornstein, column 2, lines 13-31. It would therefore have been obvious to one of ordinary skill in the art to have also developed and used a standard curve for use in comparing the results if the method described in Rice. The motivation for doing so would have been to avoid the additional time, labor, and material required to continuously repeat control assays used to determine the effect of the test assays.

Double Patenting

11. **(Prior Rejection-Maintained)** Claims 1, 4, 8, 55, and 57 were rejected in the prior action under the judicially created doctrine of obviousness-type double patenting as being unpatentable over either claims 1, 4, 7-11, 13,14,46-49,51-53,70-73, and 78-83 of U.S. Patent 5,837,464 in view of Lu et al. and Wang et al., or claims 1,2,18,24-27, and 30-42 of U.S. Patent No. 6,242,187, in view of Lu et al. or Wang et al. Claims 1,4,8,55, and 57 have been cancelled from the Application, but have been replaced by claims 112-116. Because these claims read on substantially the same subject matter, the rejection is maintained as to the new claims as applied against cancelled claims 1,4, 8, 55, and 57. The Applicant has not further traversed these rejections, but has requested that they be held in abeyance. However, the Applicant has not indicated an intent to file a terminal disclaimer. Because it is not Office practice to delay prosecution of a rejection, the request is being treated as though the Applicant had agreed to file a terminal disclaimer upon the finding of allowable subject matter in the case.

12. **(New Rejection)** Claims 112-114 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5, and 6 of copending Application No. 10/139,069. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the copending application are broader in scope than those of the present application, and therefore the applications claim overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

13. No Claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
July 10, 2003

JAMES HOUSEL 7/14/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600